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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,900	02/24/2004	Eugene R. Cooper	029318-1003	1015

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

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05/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,900	COOPER ET AL	
	Examiner	Art Unit	
	S. TRAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,16,18-52,55-57,64-72 and 74-100* is/are pending in the application.

4a) Of the above claim(s) *26-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-8,16,18-25,50-52,55-57,64-72 and 74-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/21/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

This application contains claims 26-49 drawn to an invention nonelected with traverse in the reply filed on 06/29/09. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

This application contains claims directed to the following patentably distinct species:

Surface stabilizer: a) anionic, b) cationic, c) ionic, and d) other surface stabilizer.

If other surface stabilizer is selected, please elect from: a) surface stabilizer of claim 1, b) surface stabilizer of claim 94, and c) surface stabilizer of claim 96.

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 50, 74 and 87 are generic.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would

not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Claim Objections

Claim 56 is objected to because of the following informalities: it is noted that claim 56 recited the amount of meloxicam of from about 99%, while claims 8, 78 and 92 recited the amount of meloxicam of from about 99.5%. Clarification is suggested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-8, 16, 18-25, 50-52, 55-57, 64-72 and 74-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. While the present specification discloses the term “about” for all the particle sizes recited in the claims, however, it appears that the present specification does not provide support for specific particle size of less than exactly 2000 nm, or exactly less. Similarly, it appears that the present specification does not provide support for the

amount of meloxicam being exactly at certain amount without the term "about". The specification further does not appear to provide adequate support for the exact C_{max} values without the term "about".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 80 recites the limitation "the at least one surface stabilizer" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 74 recited "surface stabilizer" is cationic, anionic or ionic. It is not exactly clear whether the surface stabilizers recited in claim 80 are in fact a cationic, anionic or ionic.

Claim 82 recites the limitation "the surface stabilizer is" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 74 recited "surface stabilizer" is cationic, anionic or ionic. It is not exactly clear whether the surface stabilizers recited in claim 80 are in fact a cationic, anionic or ionic.

Claim 95 recites the limitation "at least one cationic surface stabilizer" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 87 does not recite "cationic surface stabilizer".

Claims 16, 64, 83 and 97 recite the limitation "the C_{max}" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

Claims 1-17, 50-67, 74-83 and 87-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Struengmann et al. WO 99/09988 A1, in view of Liversidge et al. WO 9325190 a1.

Struengmann teaches a pharmaceutical composition comprising micronized meloxicam with suitable additive such as microcrystalline cellulose and/or surfactant and/or co-solvent (page 3; and examples). Surfactant is disclosed at page 4, last paragraph bridging page 5. Co-solvent includes propylene glycol, polyethylene glycol, glycerol and ethanol (page 3, last paragraph). The obtained meloxicam is then incorporated into dosage forms include controlled release oral composition, tablet, sachet, ointment, suppositories, and hydrogel (page 5, paragraphs 35).

Struengmann does not expressly teach the particle diameter of the micronized meloxicam. However, one of ordinary skill in the art would have been motivated to, by routine experiment optimize the particle size with the expectation of at least similar results. This is because it is known in the art to reduce particle size of a drug to obtain a higher bioavailability of said drug. Liversidge teaches a process of preparing nanoparticulate drug substances comprising the steps of dispersing a crystalline drug in a liquid dispersion medium containing a surface modifier, and subjecting the premix to mechanical means to reduce the particles size of the drug substance to less than 400 nm (pages 7-10). Drug includes water-insoluble drug substance such as analgesic and NSAID substances including oxicam (page 3). Surface modifier includes nonionic, anionic, organic, inorganic excipients, and mixture of two or more (pages 5-6). Surface

modifier includes polyvinyl pyrrolidone (page 6). Liversidge further teaches the surface modifier is adsorbed on the surface of the drug substance, but the individually adsorbed molecules of the surface modifier are essentially free of intermolecular crosslinkages (page 6, lines 25-31). Liversidge also teaches the nanoparticles are combined with pharmaceutically acceptable carrier suitable for parenteral injection (page 11, lines 29-35).

Thus, it would have been obvious to one of ordinary skill in the art to modify the meloxicam composition of Struengmann to obtain a nanoparticulate meloxicam composition in view of the teachings of Liversidge. This is because Liversidge teaches a nanoparticulate composition that exhibits unexpectedly rapid onset (bioavailability) (page 12, lines 11-14), because Liversidge teaches a process suitable for a wide variety of NSAIDs including oxicam, because Struengmann teaches the desirability for obtaining a composition with high bioavailability, and because Struengmann teaches reducing particle size of meloxicam by micronisation (page 3, last paragraph; page 10; and examples).

It is noted that Struengmann does not explicitly teach the claimed properties such as the C_{max} values. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation obtain the C_{max} value that falls within the claimed range, because Liversidge teaches nanoparticulate having the claimed particle size in a dispersion for parenteral injection exhibits the claimed C_{max} value, e.g., 187 µg/mL (page 16).

Claims 18-25, 68-72, 84-86 and 98-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Struengmann et al. in view of Liversidge et al., and Desai et al. WO 01/45706 A1 or Courteille et al. US 5,384,124.

Struengmann is relied upon for the reasons stated above. Struengmann does not teach the second particle population.

Desai teaches a dual-release composition of low water soluble drug (COX-2 inhibitor) comprising first fraction of the drug in nano-particulate form having average diameter of about 200 to about 400 nm and a D90 particle size less then about 5 μm (page 18); and a second fraction of the drug in micro-particulate form having D_{10} particle size of between 25 to about 100 μm (page 20, 1st paragraph). The first fraction nano-particle drug can be present alone or in combination with one or more excipient, such as nano-particles of the drug have a surface modifying agent (PEG-400) adsorbed on the surface thereof (page 18, 3rd through page 19). The weight ratio of the first to the second fraction of the drug in the composition is about 1:10 to about 10:1 (page 22, 3rd paragraph). The composition can be in an oral dosage form including tablet, pills, hard or soft capsule, lozenges, cachets, dispensable powder, granule, suspension or elixir (pages 37-38).

Courteille teaches a solid unitary composition comprising combination of nano-particle having diameter of less than 1 μm and micro-particle having diameter of between 1 μm to 2 mm (see abstract, column 2, lines 32-46). The mixture of nano/micro-particle contains one or more active agents of the same or different type (column 1, lines 66-68, and column 2, lines 23-31). The active agent can be selected

from antibiotic, analgesic, tranquilizer, vitamins, and therapeutic agents for diseases of allergies, hormones, or gastrointestinal tract (column 5, lines 46-66). The mixture of nano/micro-particle is prepared by any known method (air-fluidized bed coating, turbine coating, simple extrusion, or micro-encapsulation) employing the use of a polymer or a macromolecular substance (surface stabilizer) selected from the group of cellulose derivatives, starch, polyamide, collagen, dextrin, gelatin, polyvinyl chloride or the like (column 2, lines 46-55, and column 3, lines 18-40). The mixture further comprises stabilizing agent, surfactant, and biding agent (column 4, lines 20 through column 5, lines 1-28). Courteille further teaches the solid dosage form comprises immediate release with a secondary controlled release of mixture of nano/micro-particle (column 6, lines 16-50). The solid dosage form is to be incorporated into pharmaceutical oral dosage form (column 6, lines 51-56).

Thus, it would have been obvious to one of ordinary skill in the art to modify the composition of Struengmann to include the second particle population in view of the teachings of Desai or Courteille, because Desai and Courteille teach compositions suitable for analgesic substance, because Desai and Courteille teach that combination of one or more population of active substance with different particle size is well known in the art, and because Struengmann teaches the desirability for formulating a controlled release composition comprising different layer having different release profiles (page 5, 3-4 paragraphs).

Response to Arguments

Applicant's arguments filed 02/03/10 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615